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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,774	03/26/2001	Sunghwa Choe	2225-0020	7797

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	14

DATE MAILED: 03/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/817,774	CHOE ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *9,11-13,17 and 22-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,14-16 and 18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-39 are pending.

2. Applicant's election without traverse of Group I, claims 1-8, 10, 14-16, and 18-21 in Paper No. 12, including SEQ ID NO:30 encoding SEQ ID NO:31 corresponding to *dwf5-1*, is acknowledged. Applicant should note that the sequences set forth in the claims are separate inventions and are not species, for reasons set forth in the restriction requirement.

Claims 9, 11-13, 17, and 22-39 are withdrawn from consideration because they are drawn to non-elected inventions.

3. Claims 1-8, 10, 14-16, and 18-21 are examined in the present office action.

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See for example pages 50, 52, and 12, lines 21, 16, and 2, respectively. See MPEP § 608.01.

Drawings

5. Figure 6A and 6B need to be replaced with better quality reproductions of the gels. The RNA bands are not discernable in Figure 6B of the present copy.

Claim Objections

6. Claim 1 is objected to for reading on non-elected inventions. Applicant is requested to amend the claim to not read on non-elected inventions.

7. Objection is made to the claims for not incorporating SEQ ID NO's when referring to nucleic acid or amino acid sequences. 37 CFR 1.821(d) requires the use of the assigned sequence identifier (e.g. SEQ I.D. NO: X) in all instances where the description or claims of a patent application discuss sequences. See for example, claims 1, 4, and 6.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-8, 10,14-16, and 18-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the metes and bounds of "at least about" have not been defined. The term "at least" specifies the lowest acceptable number whereas "about" denotes an approximation of some number.

In claim 1, the recitation "complement" is unclear. Applicant has not specified "full length" complement and as such the term "complement" reads on as little as one base pair.

In claim 2, the metes and bounds of "*dwaf5* mutant phenotype" have not been defined. Applicants describe an assortment of physiological, developmental and morphological

differences between a purported *dwf5* mutant and a wild-type plant but these encompass the normal variation that is exhibited between wild-type plants (page 19, lines 6-27).

In claim 18, the term "altered" is unclear. Applicant needs to explicitly state how the phenotype has been changed.

In claim 19, the term "altered" is unclear. Applicant needs to explicitly state how the sterol delta-7 reductase activity has been changed. Does Applicant mean the reductase has been structurally altered, or that the level has been altered? Also, is Applicant referring to something that acts on the reductase or something that the reductase acts on?

Clarification and/or correction are required.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-8, 10, 14-16, and 18-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated *dwf5-1* polynucleotide, a polynucleotide comprising a nucleotide sequence having at least about 50% sequence identity to a *dwf5-1*, or DWF5 polynucleotide; a fragment of a *dwf5-1*, or DWF5 polynucleotide comprising at least about 15 contiguous nucleotides of a *dwf5-1*, or DWF5 polynucleotide; a fragment of a *dwf5-1*

polynucleotide comprising at least 30 contiguous nucleotides; a complement or reverse complement of a *dwf5-1*, or DWF5 polynucleotide; an isolated polynucleotide comprising a nucleotide sequence having at least about 50% sequence identity to the genomic DWF5 sequence and comprising at least 30 contiguous nucleotides; an isolated polynucleotide having at least about 50% sequence identity, a fragment comprising at least about 15 contiguous nucleotides or complements or reverse complements of a sequence comprising: nucleotides 1-633 of Figure 7, nucleotides 634-670 of Figure 7, nucleotides 4045-4243 of Figure 7, or a polynucleotide comprising an intron sequence as depicted in Figure 7; or an isolated polynucleotide of claim 6 comprising at least 30 contiguous nucleotides; a recombinant vector, host cell, transgenic plant and method of producing a transgenic plant and method of producing a transgenic plant having an altered phenotype.

Applicants isolated their invention by creating a mapping F2 population by crossing *dwf5-1* to Columbia wild type and selecting 50 different dwarf plants from the F2 population. Using primers DW5_3F and DW5_LR, DNA was amplified and then sequenced (page 52, 1st paragraph). Applicants do not disclose any specific structural, physical and/or chemical properties for the claimed sequence. Applicants do not present a description of domains that are specific to this particular sterol delta-7 reductase (S7R) nor domains that are important for its proper function. Given the lack of description, one skilled in the art would not be able to identify sequences with less than 100% sequence identity that still maintained the proper activity. The claims recite fragments of sequences that exhibit 50% sequence identity to a *dwf5-1* and sequences comprising as little as 15 contiguous base pairs of a *dwf5-1* polynucleotide but Applicant has not disclosed a description of a *dwf5-1* polynucleotide or what regions of the

sequence can be changed and still maintain the proper activity of the encoded protein, nor has Applicant disclosed what region(s) are essential for dwf5-1 activity. In addition, Applicant has not disclosed a representative number of species as encompassed by the claims. The claims encompass mutants and allelic variants and thus imply that structural variants exist in nature, yet no structural variant has been disclosed. The implication is that there is a gene and a protein other than that disclosed which exists in nature, but the structure thereof is not known. Therefore, there is insufficient relevant identifying characteristics to allow one skilled in the art to predictably determine which sequences exhibiting the claimed limitations would function as a *dwf5-1* polynucleotide or to determine mutants and allelic variants from other plants and organisms absent further guidance. Therefore, the written description requirement is not satisfied. Therefore, one skilled in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention. (see Written Description Requirement published in Federal Register/Vol.66, No. 4/ Friday, January 5, 2001/Notices; p. 1099-1111).

Enablement

10. Claims 1-8, 10, 14-16, and 18-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *In re Wands* factors (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one

skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to an isolated *dwf5-1* polynucleotide, a polynucleotide comprising a nucleotide sequence having at least about 50% sequence identity to a *dwf5-1*, or DWF5 polynucleotide; a fragment of a *dwf5-1*, or DWF5 polynucleotide comprising at least about 15 contiguous nucleotides of a *dwf5-1*, or DWF5 polynucleotide; a fragment of a *dwf5-1* polynucleotide comprising at least 30 contiguous nucleotides; a complement or reverse complement of a *dwf5-1*, or DWF5 polynucleotide; an isolated polynucleotide comprising a nucleotide sequence having at least about 50% sequence identity to the genomic DWF5 sequence and comprising at least 30 contiguous nucleotides; an isolated polynucleotide having at least about 50% sequence identity, a fragment comprising at least about 15 contiguous nucleotides or complements or reverse complements of a sequence comprising: nucleotides 1-633 of Figure 7, nucleotides 634-670 of Figure 7, nucleotides 4045-4243 of Figure 7, or a polynucleotide comprising an intron sequence as depicted in Figure 7; or an isolated polynucleotide of claim 6 comprising at least 30 contiguous nucleotides; a recombinant vector, host cell, transgenic plant and method of producing a transgenic plant and method of producing a transgenic plant having an altered phenotype.

Applicants' invention is SEQ ID NO:30 (*dwf5-1*) encoding a mutant sterol delta-7 reductase of SEQ ID NO:31. The *dwf5-1* mutant was isolated from a mutagensis screen of

Arabidopsis plants that had been mutagenized by T-DNA insertion. Applicants have not reduced to practice their invention. They have only described the cloning and characterization of *dwf5-1* mutant and corresponding nucleic acid sequence and they have also shown that ectopic over-expression of the *DWF5* cDNA in *dwf5-1* mutants completely converts the mutants to wild-type plants (page 63, lines 9-11).

Applicants have not taught how one skilled in the art would use plants transformed with SEQ ID NO:30 nor have Applicants taught how one skilled in the art would use SEQ ID NO:30 to generate a specific agronomically important plant. Applicants teach the importance of sterol delta-7 reductase in plant developmental and physiological processes but Applicants have not specifically addressed how a mutant *dwf* polynucleotide or a sequence comprising as little as 15 contiguous nucleotides of a *dwf5-1* polynucleotide can be used in a plant to achieve a specific phenotype or biological process. In particular, how would one use the *dwf5-1* polynucleotide to produce a plant having an altered phenotype wherein the phenotype is altered sterol delta-7 reductase activity as claimed in claims 18 and 19? It has not been taught how transforming a plant with an above mentioned sequence will produce a dominant phenotype that over-rides the wild-type activity of *DWF* especially using a sequence with 50% identity to a *dwf5-1* polynucleotide or a fragment comprising as little as 15 contiguous nucleotides of *dwf5-1* polynucleotide.

It cannot be predicted by one of skill in the art that nucleic acids exhibiting 50% sequence identity to a *dwf5-1* polynucleotide or a fragment comprising as little as 15 contiguous nucleotides of *dwf5-1* polynucleotide will encode a protein with the same activity as the wild-type DWF protein. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence

encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by McConnell et al (2001, Nature 411 (6838):709-713), who teach that the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain. This change renders the protein constitutively active and therefore creates a dominant mutation which has a drastic alteration in phenotype compared to wild-type *Arabidopsis* plants. In the present application, the *dwf5-1* allele has a single base pair deletion and renders the corresponding protein inactive (page 53, Table 2).

The state-of-the-art teaches heterologous nucleic acid molecules encoding enzymes involved in biochemical pathways does not always produce the expected results. Hamada et al (1998, Plant Physiology 118:591-598) teach that expressing heterologous desaturases in plants does not always give predictable results. Hamada et al overexpressed a tobacco microsomal ω-3

fatty acid desaturase cDNA (NtFAD3) under the control of a mosaic constitutive promoter that confers about 10-fold higher levels of constitutive expression than the CaMV 35S promoter. The results of overexpression in tobacco plants resulted in a 40% increase in alpha-linolenic acid in roots and only a 10% increase in leaves (abstract and page 593, right column, 1st paragraph of results). These results suggest that endogenous factors contribute to the observed result that can not be predicted a priori.

Therefore, given the unpredictability of using heterologous nucleic acids to alter the normal synthesis of biochemical macro-molecules for the reasons stated above; given the lack of guidance and examples of how one would use a plant transformed with a *dwf5-1* polynucleotide, how one would use a *dwf5-1* polynucleotide to generate a plant with a specific phenotype or for a specific purpose; for the reason stated above; given the breath of the claims that encompass sequences comprising as little as 15 contiguous nucleotides of a *dwf5-1* polynucleotide; and given the state-of-the-art as discussed above, undue experimentation would be required by one skilled in the art to make and/or use the broadly claimed invention.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Chenivesse et al (June, 1998, U.S. Patent Number 5,759,801).

The claims are drawn to an isolated fragment of a *dwf5-1*, or DWF5 polynucleotide comprising at least about 15 contiguous nucleotides of a *dwf5-1*; a fragment of a *dwf5-1* polynucleotide comprising at least 30 contiguous nucleotides; a complement or reverse

complement of a *dwf5-1*, or DWF5 polynucleotide; an isolated polynucleotide having at least about 50% sequence identity, a fragment comprising at least about 15 contiguous nucleotides or complements or reverse complements of a sequence comprising: nucleotides 1-633 of Figure 7; or an isolated polynucleotide of claim 6 comprising at least 30 contiguous nucleotides; a recombinant vector, host cell.

The claims are also drawn to a sequence which is a complement or reverse complement of any of the above mentioned sequences. The office interprets the 'complement' claims to read on any sequence because Applicants have not specified a sequence that is "fully" complementary to any of the above mentioned sequences. As written, a complement sequence can comprise one base pair.

Chenivesse et al teach a nucleotide sequence that comprises around 220 contiguous base pairs that are 100% identical to around 220 contiguous base pairs of the Applicants' SEQ ID NO:30. The sequence of Chenivesse et al comprises the complement of Applicants' sequence and Chenivesse et al sequence is in a vector and transformed into yeast and as such anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-8, 10, 14-16, and 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenivesse et al (June, 1998, U.S. Patent Number 5,759,801) as applied to claims 1-8, and 10 above, and further in view of Metz et al (October, 1997, U.S. Patent Number 5,679,881).

The teachings of Chenivesse et al have been discussed above. Since it is unclear what altered phenotype and altered sterol delta-7 reductase encompassed (see 112 2nd above), these limitations are not given weight here.

Chenivesse et al do not teach a method of producing a transgenic plant having an altered phenotype.

Metz et al teach *Brassica* plants transformed with a nucleic acid construct comprising a nucleic acid involved in fatty acid biosynthesis operably linked to a napin promoter (Example 8 and 9) and proteins expressed in plants (column 38, Table 4).

It would have been prima facie obvious to one skilled in the art at the time the invention was made to express the polynucleotide of Chenivesse et al in a plant using the method of Metz et al., for heterologous protein expression or enzyme expression with a reasonable expectation of success.

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist, who may be contacted at 308-0196.

Stuart F. Baum Ph.D.

February 26, 2003

PHUONG T. BUI
PRIMARY EXAMINER 2/28/03